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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,817	02/05/2004	Robert W. Marquis	PU60075	5974

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 10/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/772,817	MARQUIS, ROBERT W.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "reducing cathepsin L" with a compound of formula (I), does not reasonably provide enablement for "inhibiting cathepsin L" or "treating a disease characterized by positive selection of CD4+ T-cells by cortical thymic epithelial cells". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The instant claims are drawn to a method for "inhibiting cathepsin L" (claims 1-13) and "treating a disease characterized by positive selection of CD4+T-cells by cortical thymic epithelial cells" (claim 14) comprising administering a compound of formula (I).

The American Heritage Dictionary (Second College Edition, 1982) defines the term "inhibit" as "restrain or hold back; prevent" and "prevent" as "anticipate or counter in advance, to keep from happening". The interpretation of the instant claims allows for the complete (100%) cure, eradication, elimination or prohibition of cathepsin L (claims 1-13) by the administration of said compounds.

With respect to the scope of enablement for "inhibiting cathepsin L",

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmacy art is high. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the preventive utility of the instant compounds.

The specification discloses assay or screening method to determine cathepsin L inhibitory effects of potentially suitable inhibitors and substrates (page 15, line 29 thru page 16, line 32). However, there is no demonstrated correlation that the tests and results apply to the claimed preventive utility embraced by the instant claims.

Thus, it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" or completely cure or eradication effect.

Since the efficacy of the claimed compound(s) in prohibiting or preventing cathepsin Lmentioned above cannot be predicted from a priori but must be determined

from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to use the invention commensurate in scope with the claims.

With respect to scope of enablement of "treating a disease characterized by positive selection of CD4+ T-cells by cortical thymic epithelial cell",

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21 USPQ2d 1702, 1704-5(BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotropic hormones was unpredictable art; In re Wright, 9999 F.2d 1577, 1562, 29 USPQ d, 1570, 1513-14 (Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte Hitzeman, 9

USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or pharmaceutical activity of treating a disease characterized by positive selection of CD4+T-cells by cortical thymic epithelial cells prior to filling of the instant invention was an unpredictable art.

The claims are very broad due to the vast number of possible diseases of that are described as being "a disease characterized by positive selection of CD4+T-cells by cortical thymic epithelial cells". The instant claims cover said disease conditions that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

Although the specification discloses assay or screening method to determine cathepsin L inhibitory effects of potentially suitable inhibitors and substrates (page 15, line 29 thru page 16, line 32), the specification fails to provide sufficient guidance in how to use the invention commensurate in scope with the claims. There is no demonstrated correlation that the tests and results apply to the claimed therapeutic utility embraced by the instant claims.

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fishcher, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires

more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575.

As discussed above, considering above factors, especially the "sufficient working examples", "the level of skill in the art", "the relative skill and the unpredictability in the pharmaceutical art", "breadth of the claims" and "the chemical nature of the invention", one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the claimed compounds for the therapeutic utility encompassed by the instant claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Tew et al. (WO 02/17924 A1).

Tew teaches the use of claimed compounds represented by the formula I such as quinoline-6-carboxylic acid {(S)-naphthylen-2-yl-1-[(S)-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl carbamoyl]-ethyl}-amide (SB 468430) and quinoline-6-carboxylic acid {(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl carbamoyl]-2-phenyl-ethyl}-amide (SB 468433) for the treatment of parasitic diseases (claims).

Although Tew is silent about the activity of said compound(s) in "inhibiting cathepsin L", such property or characteristic must be inherent to the referenced compound. The prior art directing the administration of the same compound inherently possessing a therapeutic effect for the same ultimate use or purpose as disclosed by the applicant anticipates the applicant's invention even absent explicit recitation of underlying mechanism.

3. Claims 1-13 are rejected under 35 U.S.C. 102(b) as being anticipated by James et al. (The Journal of Biological Chemistry, 2001, Vol. 276, No. 15, pp. 11507-11511).

James teaches the claimed compounds represented by the formula I such as quinoline-6-carboxylic acid {(S)-naphthylen-2-yl-1-[(S)-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl carbamoyl]-ethyl}-amide (SB 468430) and quinoline-6-carboxylic acid {(S)-3-oxo-1-(pyridine-2-sulfonyl)-azepan-4-yl carbamoyl]-2-phenyl-ethyl}-amide (SB 468433) that is useful as cathepsin L inhibitor.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-14 are rejected under the judicially created doctrine of double patenting over claims 6-7 of U. S. Patent No. 7071184.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent directing the administration of the same compound inherently possessing a therapeutic effect for the same ultimate purpose (e.g., arthritis) as disclosed by the applicants anticipates the claimed invention even absent explicit recitation of the underlying mechanism. Thus, the patent makes obvious the instant invention.

5. Claims 1-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 78 and 80 of copending Application No.11/152745, claims 63 and 65 of copending Application No.11/410558 or claim 109 of copending 10/239,343. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application(s) directing the administration of the same compound inherently possessing a therapeutic effect for the same ultimate purpose (e.g., arthritis) as disclosed by the applicants anticipates the claimed invention even absent explicit recitation of the underlying mechanism. Thus, the copending application(s) make(s) obvious the instant invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. In looking in continuity data, it is noted that applicant has numerous issued patent and pending applications encompassing the same or similar subject matter of the instant application. Applicant should review all subject matter considered the same or similar, and submit the appropriate Terminal Disclaimer(s). For example, USP 6596715 and USP 6534498 are directed to same or similar subject matter(s).

Conclusion

7. No Claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have

any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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